REMARKS

I. Introduction

Applicants respectfully request reconsideration of the present reissue application of U.S. Pat. No. 6,348,481 ("the '481 patent") in view of the foregoing amendments and in view of the following reasons.

II. Status of the Claims and Summary of Amendments Thereto

After entry of the foregoing amendments, claims 1-18 will be pending. Claim 1 is amended to delete the reference to "prophylaxis." Amendments are made to claims 2 and 8 to remove references to Alzheimer's disease and indisposition. Finally, composition claim 4 is amended to delete the reference to angiotensin II mediated diseases.

Claims 11-18 are presented anew. Support for the new claims can be found throughout the specification, for example in the '481 patent at col. 14, lines 63 through col. 15, line 3 and at col. 15, lines 38-45.

III. The Office Action

A. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

1. "Prophylaxis"

Claims 1-3 were rejected under 35 U.S.C. § 112, first paragraph on the ground that the specification allegedly does not enable the claimed method as to "prophylaxis." Office Action at page 2. The amendments to the claims renders this rejection moot because the offending term has been deleted. Applicants submit in this regard that the claimed method of treatment encompasses both palliative and prophylactic treatment.

2. Diuretic and Calcium Antagonist Combinations

Claims 4 and 7 were rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement for "all and any compound having diuretic or calcium antagonistic activity." Office Action at page 3. The PTO explained that Applicants' examples of each –

namely HCT and MDP – does not reasonably provide enablement for all combinations such that the person of skill in the art would be unduly burdened to practice the invention as claimed. Applicants respectfully traverse.

Applicants' examples of the claimed composition and method of use are *exemplary* of the claimed genus of combinations of (1) one of the enumerated compounds, (2) a diuretic, and/or (3) a calcium antagonist. A person of skill in the art would understand that the use of HCT as a diuretic also pertains to other diuretics, based on common pharmaceutical activities. So, too, would the use of MDP as a calcium channel antagonist pertain to other such antagonists. Consequently, the person of skill in the art would not be unduly burdened to identify and use the claimed composition and use.

The publications collected in Appendix A further validate the claimed invention as understood by the person of skill in the art. Thus, for example, Matsumoto *et al.*, *Circulation Journal*, vol. 68 (2004) 376-382 describes the therapeutic effects of the combination of candesartan cilexetil (the first compound recited in claims 4 and 7) and spironolactone on myocardial infarction, which is an angiotensin-II mediated disease. Spironolactone is a known compound having diuretic activity, as emphasized explicitly in Applicants' '481 patent at col. 10, line 40.

Additionally, Kim *et al.*, *Hypertension*, vol. 35 (2000) 769-774 describes the therapeutic effects of the combination of candesartan cilexetil and amlodipine in hypertensive rats. *See* Kim *et al.* at 770-771 bridging. Amlodipine is a known compound having calcium antagonistic activity. *Id.*

The publications therefore further exemplify the compositions and methods as claimed. The person of skill in the art would certainly appreciate that practicing the invention, in light of the level of skill in the art as illustrated by the Matsumoto *et al.* and Kim *et al.*, would require no undue experimentation. Accordingly, combining the recited angiotensin-II receptor antagonists with either or both compounds having diuretic and calcium antagonist activity is enabled to treat angiotensin-II mediate diseases. Applicants therefore respectfully request the PTO to reconsider and withdraw the rejection.

3. Angiotensin-II Mediated Diseases

Claims 1 and 4-7 were rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement for the entire scope of claimed angiotensin-II mediated diseases. Office Action at page 4. The PTO added that only some diseases, such as hypertension and other circulatory diseases, are enabled. Applicants respectfully traverse.

As an initial matter, the rejection of composition claims 4-6 is improper because the specification offers extensive teaching on the compositions *per se*. *See* the '481 patent at col. 10, line 62 to col. 14, line 35. In any event, claims 4-6 do not recite angiotensin-II mediated diseases.

Second, the ground for rejection here is wholly inconsistent with PTO's examining and allowing method claims reciting "angiontensin-II mediated disease" *in the very patent on which Applicants now seek reissue*. In this regard, the PTO examined and allowed similar method claims reciting "angiotensin-II mediated disease" in commonly assigned U.S. Pat. No. 6,107,323 (*see* claims 1 and 7; copy provided in Appendix B). Applicants therefore request the PTO to reconsider and withdraw this ground for rejection.

B. Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph

1. "Indisposition" and "Including"

Claims 2 and 8 were rejected under 35 U.S.C. § 112, second paragraph as being allegedly indefinite for reciting the terms "indisposition" and "including Alzheimer's". The cancellation of the terms by way of the present amendments renders this ground for rejection as moot. In this regard, Applicants understand that the recited "sensory disturbances" encompasses diseases such as Alzheimer's disease.

2. "Mediated"

Claims 1-10 were rejected 35 U.S.C. § 112, second paragraph as being allegedly indefinite for reciting the term "mediated", which, in the PTO's analysis, ambiguously refers to a direct or an indirect mechanism. Applicants respectfully traverse the rejection.

The term "mediated" is well understood in the context of the pharmaceutical and medicinal arts. As taught throughout the specification, the recited compounds are angiotensin-II antagonists, which inhibit angiotensin-II receptors. The resultant effect is the treatment of diseases arising from the presence of angiotensin-II. The person of skill in the art would therefore harbor no uncertainty as to the definition of the term "mediated".

C. Rejection of Claims Under Obviousness-Type Double Patenting

Claims 1-10 were rejected as being allegedly obvious over claims 1-8, 1-15, and 1-3 of U.S. Pat. Nos. 5,721,263; 5,958,961; and 6,228,874, respectively, under the doctrine of obviousness-type double patenting. Office Action at page 6. Applicants respectfully acknowledge the rejection, but in light of the other pending issues, Applicants kindly defer a substantive treatment of obviousness-type double patenting, if it remains an issue at all, until such time as the PTO indicates allowable subject matter.

D. Rejection of Claims Under 35 U.S.C. § 103(a)

Claims 1-10 were rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over EP 0459136 to Naka *et al.* ("Naka") in view of EP 0400835 to Chakravarty *et al.* ("Chakravarty"). Office Action at pages 7-8. The PTO cited Naka for its disclosure of the claimed benzimidazole compounds for use in treating hypertension. The PTO relied upon Chakravarty for its alleged teaching of "essentially the same" benzimidazole compounds in combination with diuretics or calcium channel blockers for the same use. Applicants respectfully traverse.

The quoted phrase above points up there being absolutely no suggestion in the references or otherwise that would have motivated the person of ordinary skill to make the specific combinations as claimed. Thus, while Naka may teach the claimed benzimidazole compounds, it does not teach the combination and uses of those compounds with a diuretic and/or a calcium channel blocker.

Chakravarty discloses a genus of benzimidazole compounds (Formula I) optionally in combination with a diuretic and/or a calcium channel blocker. Chakravarty does not teach or

suggest, however, the instantly claimed benzimidazole compounds. One cannot manufacture from Chakravarty a suggestion pointing toward the specifically claimed compounds, as here, merely on the basis of the refernece disclosing a genus of compounds. Thus, "essentially the same" falls short of the requisite motivation to combine the references in a way that at least suggests the specifically claimed benzimidazoles in combination with a diuretic and/or a calcium channel blocker. Because the references engender no such motivation, and because the PTO has identified none, Naka and Chakravarty cannot support the rejection. Consequently, the claims are patentable over the cited combination.

Notwithstanding these considerations, Applicants kindly note with respect to claims 1-3 that this Examiner allowed composition claims of identical scope in the parent application, now U.S. Pat. No. 6,228,874. Because the PTO granted these claims, Applicants respectfully submit that no reason exists why the present method claims should not also be allowable.

Additionally, Kim, *supra*, evidences unexpected effects of the claimed subject matter. Specifically, Kim describes that monotherapy of 0.2mg/kg candesartan cilexetil of 0.5 mg/kg amlodipine failed to reduce the cardiac mRNAs of the SHRSP (data not shown). However, Kim further disclosed that the *combination* of these drugs significantly decreased left ventricular mRNA levels for ANF, skeletal α-actin, and collagen types I and II. Thus, even if Chakravarty and Naka could be combined, a proposition that Applicants do not endorse, these data validate therapeutic effects of the claimed combinations that are unexpected in view of the cited combination.

For all of these reasons, the claims are patentable over Naka and Chakravarty. Accordingly, Applicants respectfully request the PTO to reconsider and withdraw the rejection.

E. Rejection of Claims Under 35 U.S.C. § 251

Claims 4-10 are rejected under 35 U.S.C. § 251 for recapture of subject matter that was allegedly surrendered in distant parent application serial nos. 08/254,541 ("the '541 application") and 08/351,011 ("the '011 application") "to overcome a 112/1 rejection."

Office Action at pages 8-9. The rejection pertains specifically to the terms "diuretic", "calcium channel antagonists or blocker," and "angiotensin II-mediated diseases." Applicants respectfully traverse.

The rejection is moot as to the '541 application because no claims were amended or cancelled during the pendency of that application, which is now abandoned. Thus, prosecution of the '541 application cannot trigger recapture.

The rejection is improper because it is based upon Applicants' alleged actions during the prosecution of distant application family members and not upon the application for the patent upon which the present reissue is based. Here, the '481 patent matured from application ser. no. 09/758,355, which was allowed on the first office action. Applicants did not surrender subject matter then, so recapture does not pertain now.

The rejection is further improper because the event giving rise to the alleged surrender of subject matter in the '011 application was Applicants' response to a non-prior art ground for rejection. The PTO's guidelines for determining whether recapture exists are replete with directives to evaluate whether or not an applicant amended or cancelled claims to define the claims over the art or overcome an art rejection of record. *See* MPEP § 1412.02 at 1400-22 (Rev. 2, May 2004; recapture analysis flow chart). In the '011 application, as the PTO correctly noted, Applicants amended the claims to overcome a section 112, first paragraph rejection. Because this is not a ground for the surrender of subject matter for purposes of recapture, Applicants respectfully request the PTO to reconsider and withdraw the rejection.

IV. Conclusion

Applicants believe that the present reissue application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if she feels that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

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The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.